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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,333	08/23/2004	Rodolfo Cadilla	PU4675USW	3786

23347 7590 10/26/2005

GLAXOSMITHKLINE
CORPORATE INTELLECTUAL PROPERTY, MAI B475
FIVE MOORE DR., PO BOX 13398
RESEARCH TRIANGLE PARK, NC 27709-3398

EXAMINER	
ROBINSON, BINTA M	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 10/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/505,333	CADILLA ET AL.	
	Examiner	Art Unit	
	Binta M. Robinson	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-20* is/are rejected.

7)☒ Claim(s) *1-17, 21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Claims 1-21 are objected to because the term "cycloakyl" in line 1 of claim 1, line 6, page 2 is misspelled. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of the diseases stated in claim 19 other than heart failure, is not enabled for the prevention of any disease or condition associated with on or more of human PPAR alpha, gamma, or delta ("hPPARs"), for the treatment of heart failure or the treatment of all diseases or conditions associated with on or more of human PPAR alpha, gamma, or delta ("hPPARs") . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The Nature of the Invention

The nature of the invention in claims 18-20 is the treatment of any disease or condition associated with one or more human PPAR alpha, gamma, or delta with the compound of claims 18-20.

The State of the Prior Art

The state of the prior art is that Peroxisome Proliferator Activated Receptors (PPARs) are receptors belonging to the steroid/retinoid receptor superfamily of ligand-activated transcription factors. See page 1 of the specification, line 27-29. It has been reported that thiazolidinediones are potent and selective activators of PPAR-gamma and bind directly to the PPAR-gamma receptor. See page 2 of the specification, lines 4-5. Rosiglitazone, a peroxisome proliferator-activated receptor gamma receptor activator must be administered with caution to patients having heart failure since the drug has been associated with elevations of total, LDL, and HDL cholesterol during clinical trials. See Hcaplus 134:125379. The role of PPAR-gamma in heart failure is controversial. See page 2 of Thiemermann. On the one hand, PPAR-gamma ligands reduce the hypertrophy caused by mechanical strain in neonatal cardiac myocytes. See page 2 of Thiermermann et. al. However, there is clinical evidence of an increase in the incidence of heart failure in patients with type II diabetes who are treated with thiazolidinediones. See page 2 of Thiemermann. PPAR-*y* activators may trigger an aggravation of congestive heart failure. Caution has been urged in the use of thiaolidinediones in diabetic patients with advanced heart failure. See page H 1040 of Schriffin.

The predictability or lack thereof in the art

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of PPAR-mediated diseases, whether the PPAR was activated or not would affect the possible treatment of any disease.

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by the claimed and the activation of PPAR, one of skill in the art is unable to fully predict possible results from the administration of the claimed compound due to the unpredictability of the role of PPAR, i.e. whether activation would be beneficial for the treatment of the diseases.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present

The direction present in the instant specification is that the compounds of claim 18-20 can activate PPAR which helps in the treatment and prevention of diseases associated with one or more human PPAR alpha, gamma, or delta. However, the specification fails to provide guidance as to whether the diseases listed as human PPAR-mediated diseases, require the activation of PPAR and fail to provide a correlation between the diseases listed and the activation of PPAR.

The presence or absence of working examples

There are no working examples for any diseases listed in the specification. Also, the compounds which are disclosed in the specification have no pharmacological data regarding the treatment of any other disease besides the rejection of an organ transplantation and have no data on the possible treatment of PPAR-mediated diseases that require the activation of PPAR. Also, the specification fails to provide working examples as to how the listed diseases can be treated by the activation of PPAR, i.e. again, there is no correlation between the diseases listed and activation of PPAR.

The breadth of the claims

The breadth of the claims is that the compound of claims 18-19 can treat any PPAR-mediated disease, without regards as to the affect of PPAR on the stated diseases.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what listed diseases would be benefited by the

activation of PPAR and would furthermore then have to determine whether the claimed compounds would provide treatment of the disease by the activation of PPAR.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the claims 18-20 for the treatment of any PPAR-mediated disease. As a result necessitating one of skill to perform an exhaustive search for which PPAR-mediated diseases can be treated by the compound of claims 18-20 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which PPAR-mediated diseases can be

treated by the compound encompassed in the instant claims, with no assurance of success.

The IDS filed 8/23/04 has been considered. The references that have been crossed out will not be considered until provided to the examiner.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (703) 306-5437. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Cecilia Tsang can be reached on (571)272-0692. The fax phone numbers for the organization where this application or proceeding is assigned are (703)308-7922 for regular communications and (703)308-7922 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0193.

BMR
October 21, 2005

Cecilia J. Tsang
Supervisory Patent Examiner
Technology Center 1600